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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,955	07/07/2003	Hirohiko Tsuzuki	Q76105	4760

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SUGHRUE MION, PLLC  
2100 PENNSYLVANIA AVENUE, N.W.  
SUITE 800  
WASHINGTON, DC 20037

EXAMINER

SINGH, SATYENDRA K

ART UNIT PAPER NUMBER

1651

DATE MAILED: 09/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/612,955	TSUZUKI ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Satyendra K. Singh	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 28 June 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 12-15 and 17-19 is/are pending in the application.
- 4a) Of the above claim(s) 16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 12-15 and 17-19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 28<sup>th</sup> 2006 has been entered.

Claims 12-19 are pending in the instant application.

Claim 16 is withdrawn from further consideration as non-elected invention.

Claims 1-11 and 20 have been cancelled by applicant's amendment to the claims.

Claims 12-15 and 17-19 are being currently examined on their merits, herein.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being **indefinite** for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claimed invention is drawn to "a carrier for cell culture comprising water-containing gel comprising alginic acid, wherein a surface of the carrier is coated with collagen, and wherein the collagen is bound to a surface of the water-containing gel by means of chitosan", which is confusing. The claimed invention is

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indefinite as the **structural features** of the cell culture carrier, as claimed, are not clear because the **shape** as well as the **spatial relationships** between various elements (such as collagen, alginic acid, and chitosan) have not been clearly specified.

Appropriate explanation/correction is required.

Since, claims 13-15 and 17-19 depend (directly or indirectly) from the broader claim 12, they are also rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 12-15 and 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hara et al (U.S. Patent 6,821,107 B1, [A]) in view of Huguet & Dellacherie [U] and Clapper et al (U.S. Patent 5,512,474 [B]).

Claims 12-15 are drawn to a carrier for cell culture that comprises a water-containing gel comprising alginate or alginate/polylysine, wherein a surface of the carrier is coated with collagen, and wherein the collagen and the water-containing gel containing alginate are presumed to be intermediated by a layer of chitosan (see rejection, supra), and wherein the alginate containing carrier for cell culture is formed on a porous membrane.

The carrier for cell culture, as claimed in the present invention, is formed on a porous membrane and comprises of a layer of alginate gel coated with collagen containing an intermediate layer of chitosan between alginate gel layer and collagen coating, and may enable culture (as well as visualization) of mammalian cells (anchorage-dependent or adherent cultures) on the collagen layer using various culture media and conditions used for standard cell culture.

Claims 17-19 are drawn to a method for culturing cells and a cell culture obtained by such method using the carrier for cell culture as claimed in claim 12.

Hara et al [A] teach a carrier for cell culture comprising an alginate gel layer (calcium alginate as claimed in the instant claim 13) formed on a porous membrane (as claimed in the instant claim 15) having an extracellular matrix component gel layer (made of collagen) or extracellular matrix component sponge layer formed on the alginate gel layer (see Hara et al, abstract, fig. 1 and 2, summary of the invention, and example 1, in particular). Hara et al [A] also teach a method for culturing cells, a method for producing cell culture, and a cell culture obtained by the methods using the carrier for cell culture where the cell layer is formed on the extracellular matrix

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component gel layer or extracellular matrix component sponge layer or on the alginate gel layer by the method step of allowing the cells to grow and form a cell layer on the surface of the carrier for cell culture (see Hara et al, example 2, in particular). In addition, the alginate gel layer is solubilized using chelating agent to exfoliate cell layer from the porous membrane, and the exfoliated cell layer is further laminated on another cell layer on a carrier providing a method of forming a structure having multiple cell layers (see Hara et al, abstract, fig 1 & 2, summary, and examples 2-3, in particular).

However, a carrier for cell culture, wherein the collagen layer is bound to a surface of the water-containing gel (comprising alginic acid or alginate) by means of **chitosan as an intermediate layer** is not explicitly taught by Hara et al [A].

Huguet & Dellacherie [U] teach a microcapsule (suitable for microencapsulation of biological materials, including cells) comprising calcium alginate beads that are coated with chitosan as an outermost layer in order to study the rate of release of biological materials such as proteins, and dextran (having different molecular weights) from the encapsulated beads (see Huguet & Dellacherie, abstract, introduction, methods, pages 745-746, in particular and references therein).

In addition, Clapper et al [B] teach a cell culture system comprising a support material providing a surface for the attachment of cells (for the purpose of anchorage-dependent cell culture) comprising a stable combination of positively charged molecule (chitosan) and cell adhesion factor (collagen) (see Clapper et al, abstract, summary, column 3-4, in particular).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the carrier for cell culture of Hara et al [A] (and therefore, the methods steps for culturing and producing the cell culture using such modified carrier) comprising an alginate gel layer formed on a porous membrane which is further coated with a collagen layer, such that the collagen gel layer is bound to a surface of alginate by means of a polycationic polysaccharide (such as chitosan) as explicitly taught by Huguet & Dellacherie [U] and Clapper et al [B].

The person of ordinary skill in the art would have been motivated to make that modification in the carrier for cell culture (and therefore, the methods steps dependent on it) by incorporating an intermediate layer containing chitosan (which is bound to the layers of collagen and water-containing gel containing alginate) because: 1) Huguet & Dellacherie disclose the benefits of coating calcium alginate with chitosan in order to providing strength and reinforcement to the water-containing gel (alginate gel) layer (see Huguet & Dellacherie, page 745, abstract and introduction, in particular); and -2) Clapper et al [B] explicitly disclose the benefits of using polycationic or positively charged molecule (chitosan or polylysine) in combination with cell adhesion factor (collagen, etc.) bound to the surface of a cell culture support of a bioreactor to improve cell attachment and stabilize cell growth (see Clapper et al, abstract, summary, and column 3-4, and examples, in particular).

One of ordinary skill in the art would have had a reasonable expectation of success when modifying the carrier for cell culture (and therefore, the attendant method steps using such modified carrier for cell culture) as taught by Hara et al by

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incorporating an intermediate layer of chitosan (between the layers of water-containing alginate gel and collagen) as taught by Huguet & Dellacherie and Clapper et al because the prior arts explicitly teach the method steps involved in the preparation and use of chitosan for coating the alginate gel layer as well as the method for the providing coating of chitosan and collagen on a cell culture support system for obtaining enhanced cell attachment in anchorage-dependent cell culture systems.

Even though the shape of the cell culture carriers disclosed by both Huguet & Dellacherie and Clapper et al may be different than the instant invention (which is not clearly defined, see rejection and discussion, supra), the method steps required to form layers of collagen and chitosan are same, and therefore, are immaterial to the benefits associated with such modification in the carrier for cell culture (as taught by Hara et al) using chitosan as an intermediate layer between alginate gel layer and collagen layer.

Since, the benefits accruing from such a modification would provide an effective, biocompatible, reinforced support system for use in cell culture methods for mammalian cells that may require transfer of the cell culture product, lamination of the cultured cell layers, and formation of multilayered cell structures resulting in three-dimensional tissue structures (as disclosed by Hara et al, see column 7, first paragraph, in particular), one of ordinary skill in the art would be motivated to combine the teachings of the Huguet & Dellacherie and Clapper et al with the teachings of Hara et al to modify their carrier for cell culture (and hence the methods using that carrier) as claimed in the present invention.



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As per MPEP, *"The selection of a known material based on its suitability for its intended use supported a prima facie obviousness determination in Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945)"* (see MPEP 2144.07).

Thus, the invention as a whole would have been *prima facie* obvious to one skilled in the art at the time the claimed invention was made.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

*A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.*

*Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).*

Claims 12-15 and 17-19 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over 1-6 of U. S. Patent No. 7,022,523 B2 (issued on April 4<sup>th</sup> 2006 to common inventors and assignee, Fuji Photo Film Co., Ltd.). Although the conflicting claims are not identical, they are not patentably distinct from each other because both US Patent '523 and the instant application claim a cell culture carrier comprising a water-containing gel containing chitosan, wherein the water-

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containing gel is coated with collagen and/or alginic acid (see claim 1 in the US Patent '523, in particular), which fully encompasses the scope of the claimed invention presented by applicants in the instant invention.

### ***Response to Applicant's Arguments***

Claims 12-15 and 17-19 are rejected under 35 U.S.C. 103(a) as being obvious over Hara et al (U.S. Patent 6,821,107 B1, [A]) in view of Huguet & Dellacherie [U] and Clapper et al (U.S. Patent 5,512,474 [B]).

Applicant's arguments (see applicant's remarks filed on June 1<sup>st</sup> 2006, pages 5-7, in particular) were fully considered but were not found to be persuasive. As mentioned in the advisory notice sent to the applicants (mailed on June 9<sup>th</sup> 2006), applicant's arguments that use of chitosan in the invention as claimed provides an unexpected superiority (by providing transparency to the cell culture carrier) over the cited prior art invention of Hara et al (in view of teachings from Huguet & Dellacherie and Clapper et al) is unpersuasive because the physical property of the chitosan gel as argued can not be an unexpected result, rather an intrinsic property of the chitosan polymer itself. Moreover, the structural limitations that applicants are arguing about are not required by the invention as claimed (see recitations of the instant claim 12-15, in particular).

### ***Conclusion***


NO claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyendra K. Singh whose telephone number is 571-272-8790. The examiner can normally be reached on 9-5MF (alternate Fridays OFF).

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

  
Satyendra K. Singh  
Patent Examiner  
Art Unit 1651

  
SANDRA E. SAUCIER  
PRIMARY EXAMINER